Sixth Quarterly Progress Report

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Feasibility of an Intra-Neural Auditory Prosthesis Stimulating Electrode Array

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1. Introduction

The objective of this research is to evaluate the feasibility of intra-neural stimulation as a means of auditory prosthesis. We are stimulating the auditory nerve with penetrating multi-channel electrode arrays and monitoring the tonotopic spread of activation in the central nucleus of the inferior colliculus (ICC) of cats.

2. Summary of activities for the quarter

In the present quarter, the P.I. presented our ongoing work in a podium presentation at the Neural Interfaces Workshop in Bethesda (August 21-23, 2006). We submitted for publication a manuscript describing ICC responses to intra-neural electrical stimulation using a lateral, trans-cochlear approach. That manuscript is being transmitted to the NIH Program Officer as an appendix. We conducted acute physiological experiments in four cats using an intra-cranial approach to the auditory nerve. In those experiments, we recorded ICC responses to acoustic and intra-neural-electric stimulation and recorded auditory nerve responses to acoustic stimulation. The principal accomplishments of those experiments were the following:

- *Refinement of intra-cranial approach to the auditory nerve.* In all of the experiments for this research program, a 32-channel recording probe is inserted into the right inferior colliculus, adjusted in position according to the responses to acoustic tones, and then fixed in place. In previous experiments using a lateral approach to the left auditory nerve, the recording probe has been fixed in place prior to exposure of the left cochlea. In the first of the recordings conducted this quarter using an intra-cranial approach to the nerve, however, we observed a shift in the ICC tonotopic map relative to the recording probe. That shift apparently resulted from a small displacement of the brainstem resulting from gentle retraction of the brainstem to visualize the auditory nerve. To avoid that problem in subsequent experiments, we made the preliminary exposure of the auditory nerve and cochlear nucleus region prior to fixing the recording probe in place. We preserved the animal's hearing in these experiments, so it was possible to confirm the tonotopic stability of ICC recordings throughout each experiment. Another refinement in the intra-cranial nerve stimulation was that we were careful in these experiments to align the silicon-substrate stimulating array such that the plane of the array was parallel to the longitudinal axis of auditory nerve fibers. Inattention to that alignment might have accounted in part for the broad or bi-lobed tonotopic spread of excitation that we often observed in the first of our experiments using the intra-cranial approach (described in QPR5).
- *Functional topography of intra-neural stimulation sites.* As in the experiments described in QPR5, the topography from intra-neural stimulating sites to ICC tonotopic place was complex and variable among stimulating-array placements in each animal and among animals. Using the intra-neural approach, we often observed restricted activation of low-frequency fibers and somewhat more restricted activation of middle-frequency fibers than we observed using the lateral approach to the nerve. Conversely, we seldom observed restricted activation of the very-high-frequency fibers that we commonly observed with the lateral approach. We assume that the absence of high-frequency activation simply reflects our present lack of understanding of the detailed functional geometry of the intra-cranial portion of the nerve. We intend to explore this further in our next series of experiments.
- *Recordings of auditory-nerve responses to sounds.* In each of the animals studied this quarter, we were successful in preserving hearing while exposing the nerve. Using the

silicon-substrate intra-neural electrodes both for stimulation and for recording, we alternately (1) recorded auditory nerve responses to tonal stimuli and (2) stimulated the auditory nerve electrically while monitoring frequency-specific activation of the ICC. On line, spike activity from the nerve often was masked by a strong sound-evoked waveform that we take to be the auditory neurophonic. Off line, we characterized that waveform precisely by averaging across the responses to 20 repetitions of each stimulus condition, then we subtracted the averaged waveform from each individual neural trace to reveal unit spike activity. Responses recorded from the auditory nerve using silicon-substrate electrodes ranged from robust multi-unit spike activity to well isolated single units (at about 10% of recording sites). Recordings from the auditory nerve yielded the familiar V-shaped frequency response areas. Figure 1 shows frequency response areas recorded simultaneously from 16 intra-neural sites. Superficial to deep recoding sites are show in panels progressing from top to bottom and then left to right.

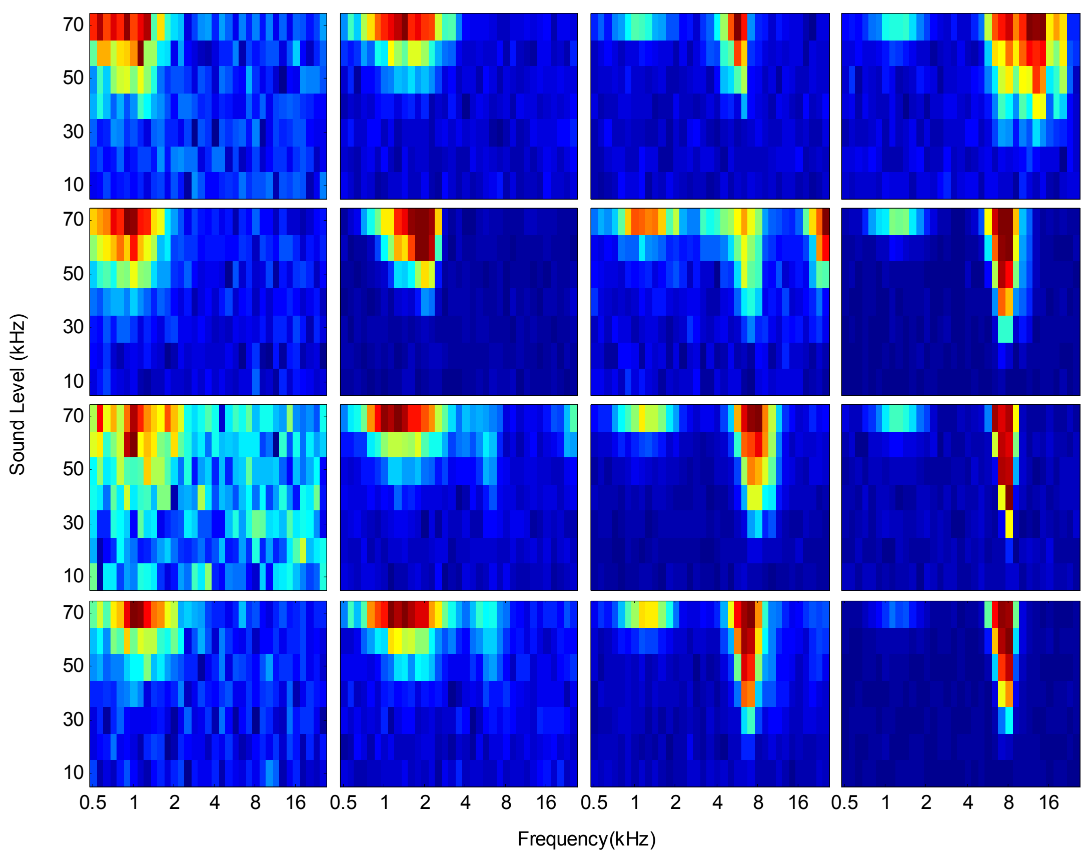

Figure 1: Frequency response areas recorded from the auditory nerve using acoustic tonal stimulation. Each panel represents the frequency tuning of single- or multi-unit activity recorded at one intraneural site.

In some cases, the spread of activation in the ICC resulting from electrical stimulation at a particular intra-neural site was substantially broader than that expected from the frequency sensitivity recorded at that intra-neural site. Alternatively, the ICC activation pattern could show 2 discrete lobes, each lobe tonotopically restricted but only one located at the expected

ICC tonotopic site. An example of such a situation is shown in figure 2. In this example, a single well-isolated unit was recorded at an intra-neural recording site. That unit was tuned to a characteristic frequency (CF) of 2 kHz (Fig. 2A). A 2-kHz tone elicited a restricted spatial tuning curve in the ICC (Fig. 2C). Electrical stimulation at the same intra-neural site, however, elicited a bi-lobed ICC spatial tuning curve (Fig. 2B). One of the lobes encompassed the 2-kHz region and the other lobe lay at a high-frequency ICC region. We infer that in this example, the intra-neural recording/stimulation site was located in a fascicle containing fibers from the 2-kHz cochlear region and that electrical stimulation spread to a nearby fascicle containing high frequency fibers from the cochlear base.

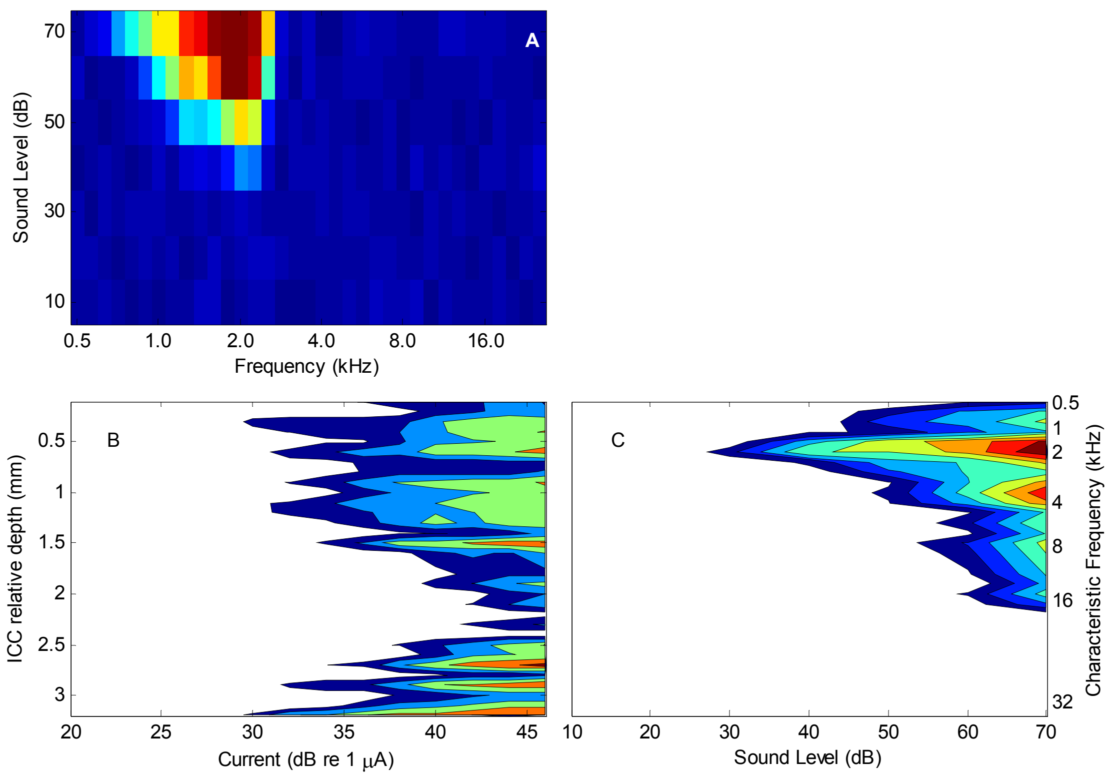

Figure 2: Correspondence of acoustic frequency sensitivity and topography of electrical stimulation. The characteristic frequency was ~2.0 kHz. A: Frequency response area recorded at one intraneural site using acoustic tonal stimulation. B: Spatial tuning curve recorded in the ICC in response to single-pulse electrical stimulation at the same intraneural site. Two lobes correspond in tonotopic place to ~2 and ~32 kHz. C. Spatial tuning curve recorded in the ICC in response to acoustic stimulation with a 2-kHz tone.

In other cases, spread of activation in the ICC resulting from intra-neural electrical stimulation was as or more restricted than the response to an acoustic tone. Figure 3A shows the frequency response area of a well-isolated single unit recorded in the nerve. The CF was ~8 kHz. Acoustic stimulation with an 8-kHz tone produced the restricted ICC spatial tuning curve shown in Fig. 3C. Electrical stimulation at the intra-neural site elicited the ICC spatial tuning curve shown in Fig. 3B. That electrical-elicited tuning curve was closely aligned in the ICC with the response to a tone equal in frequency to the CF measured at the auditory nerve recoding/stimulation site.

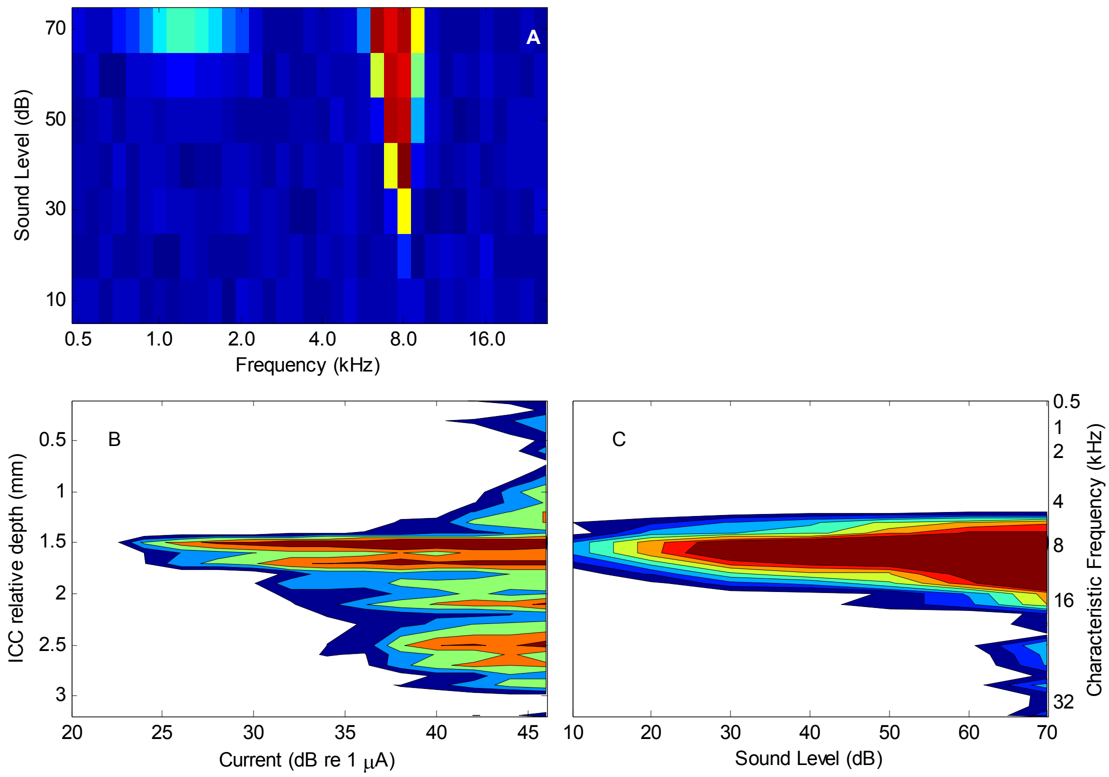

Figure 3: Correspondence of acoustic frequency sensitivity and topography of electrical stimulation. The characteristic frequency was ~8.0 kHz. A: Frequency response area recorded at one intraneural site using acoustic tonal stimulation. B: Spatial tuning curve recorded in the ICC in response to single-pulse electrical stimulation at the same intraneural site. The single lobe corresponds in tonotopic place to ~8 kHz. C. Spatial tuning curve recorded in the ICC in response to acoustic stimulation with an 8-kHz tone.

3. Plans for next quarter:

- Extend study of functional topography of the auditory nerve using the intra-cranial approach.
- Meet with otologic surgeons in our department to consider surgical approaches that could be used in humans. We hope that human cadaver material can be obtained and demonstration dissections performed during this quarter. These dissections will be crucial to translation of intra-neural stimulation to human trials. Based on the empirical experience of the surgeons, results of these dissections, and on the results from our animal model regarding lateral and intra-cranial approaches to the auditory nerve, we hope to be able to make recommendations on the best approaches to intraneural stimulation in humans and to focus our continuing experiments on those approaches.
- If custom chronic probes become available, test ICC recording through the new guide-tube system.